UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/058,655	01/28/2002	Albert S. Benight	13534-002001	3865

26161 7590 11/30/2004

FISH & RICHARDSON PC
225 FRANKLIN ST
BOSTON, MA 02110

EXAMINER	
DEJONG, ERIC S	
ART UNIT	**PAPER NUMBER**
1631	

DATE MAILED: 11/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	Application No.	Applicant(s)	
	10/058,655	BENIGHT ET AL.	
	Examiner	Art Unit	
	Eric S. DeJong	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *18-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☒ Claim(s) *11,17* is/are objected to.

8)☒ Claim(s) *1-28* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Election/Restrictions

Applicant's election without traverse of Group I (claims 1-17) in the reply filed on 22 September 2004 is acknowledged. Claims 18-28 are withdrawn from further consideration.

Priority

The incorporation by reference of [Duca and Hopfinger (2001), J Chem Inf Comput Sci 41(5):1367-87; Kulkarni and Hopfinger (1999), Pharm Res 16(8): 1245-53; Kulkarni et al.(2001), Toxicol Sci 59(2) 335-45; The Chem21 Group, Inc. manuals regarding QSAR on page 49, lines 5-7 of the Specification; Yazdanian et al. (1998), Pharmaceutical Research 15:1470-94; Kulkarni and Hopfinger et al. (1999) Pharmaceutical Research 16:1244-52 and J.W. McFarland et al. (2001) J Chem Inf Computer Sci 41(5):1355-9] contains material provided for in the non-provisional application 10/058,655 but not provided for in the provisional application 60/264,640, to which priority is claimed. As such, any claims of said non-provisional application enabled only by the essential materials from the above references will not be granted benefit of said provisional application filing date.

In the instant case, said provisional application includes reference to [Walters et al. (1998) Drug Discovery Today, 3:160-94; Hopfinger et al. (1999), Chem Inf Comput Sci 39:1151-60, Hopfinger et al. (2000) Curr Opin Biotech 11:97-103; Duca and Hopfinger (2000), Chem of Materials, 10: 876-85; Tokarski et al. (1997), Chem Inf Computer Sci 37L792-811 and Venkatarangan and Hopfinger (1999), J Med Chem 42:2169-79] that is sufficient to establish benefit of priority to said provisional application

filing date for claims 1-7, 11 and 13-17 from said non-provisional application. Exceptions are made for claims 8, 9 and 10 (claims that involve a 4D-QSAR model) and claim 12 (the claim that involves a MI-QSAR model) as enabling descriptions of 4D-QSAR and MI-QSAR are not disclosed by the references provided in said provisional application, but rather by the cited references [Duca and Hopfinger (2001), J Chem Inf Comput Sci 42:1367-87] and [Kulkarni and Hopfinger (1999), Pharm Res 16(8): 1244-52 and Kulkarni et al.(2001), Toxicol Sci 59(2) 335-45] from said non-provisional application. Claims 8, 9, 10 and 12 will not be granted benefit of priority to the provisional application filing date.

Claim Objections

Claim 11 is objected to because of the following minor spelling error: in claim 11, line 1 the phrase "at least one the modules" should be replaced with -- at least one of the modules --.

Claim 17 is objected to because of the following minor spelling error: in claim 17, line 5 the word "form" should be replaced with -- from --. Appropriate corrections are required.

Claim Rejections - 35 USC § 112

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at

1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 6-17 are rejected under 35 U.S.C. 112, first paragraph.

A reasonably broad interpretation of the phrase "describing the interaction" as set forth in claims 1, 6, and 16 is not limited to descriptors derived only from empirical measurement. The specification, while being enabling for a set of data obtained by an instrument describing the interactions between each training compound of the set and an interaction partner consisting of physical, chemical, or biological observables (for example elements of a chemical structure, measurements of enthalpy, or changes in the extinction coefficient for a given frequency of light), does not reasonably provide enablement for a set of data comprising subject matter outside of empirical

determination (for example cost or availability of a given compound) or subject matter pertaining to aesthetic properties (for example smell). The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to manufacture and/or use the invention commensurate in scope with these claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8, 11-15, and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The use of the abbreviated terms 4D-QSAR (instant claim 8), ADMET (instant claims 11, 12, 13, 15, and 17), MI-QSAR (instant claim 12), and Caco-2 (instant claim 14) causes the claims to be vague and indefinite and should be accompanied by an explicit definition when first recited in a set of claims. For example, "membrane interaction quantitative structure-activity relationship (MI-QSAR) model" would be acceptable claim language. Use of abbreviated terms in a claim which follow an explicit definition in preceding claims is acceptable. Appropriate corrections are required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 6, and 16 are rejected under 35 U.S.C. 102(e)(2) as being clearly anticipated by Agrafiotis et al.

Instant claim 1 requires obtaining a set of data describing the interaction between each member of a set of training compounds and an interaction partner, along with data about chemical structure and/or physical properties, for use in constructing a module to predict values describing the interaction between a chemical compound and the interaction partner. Agrafiotis et al. teaches obtaining physical, chemical and/or biological data pertaining to selected compounds, as well as their related structural properties, for use in constructing and operating an iterative computational module to predict physical properties of a compound. See Agrafiotis et al., abstract.

The instant application discloses several biological examples of interacting molecules, however the definition put forth in the specification as to what the training compounds and interacting partners may be is summarized by the limitation that they are molecules known to interact with one another. Agrafiotis et al. provides a specific example embodiment of the disclosed invention involving thrombin binding to several inhibitors. See Agrafiotis et al., column 9, lines 7-33. This example demonstrates that selecting molecules known to interact with one another, such as the ligand-receptor pair embodied in inhibitor-thrombin binding, are suitable for use in the methods disclosed by Agrafiotis et al.

The instant application discloses construction of a module that predicts values describing the interaction between a compound and interaction partner consisting of one or more scoring functions that incorporate a set of data describing the interaction between training compound and interaction partner and may further incorporate the physical structure and/or physical properties of the compound. The iterative computational module disclosed in Agrafiotis et al. incorporates data on selected compounds, for example a ligand-receptor pair, for use with one or more structure-property models, which the instant application discloses as a suitable type of scoring function, to predict properties that one or more compounds posses. See Agrafiotis et al. Column 11, lines 8-21. The predicted values returned by the module, as set forth in claim 1 must be of the same type of data as the data contained in the set of data used to construct the module. Agrafiotis et al. teaches that values returned by the iterative computational model may be of the type used in constructing the module. See Agrafiotis et al., column 13 line 65 to column 14 line 32.

Instant claim 2 requires that the first data set be obtained experimentally by a high throughput instrument. Though examples are included, the instant application does not provide a specific definition for a high throughput instrument. A reasonably broad interpretation of a high throughput instrument is an instrument that is designed to perform an automated series of experiments after being furnished with multiple samples. Agrafiotis et al. provides for alternative methods of analyzing and acquiring data for use in the invention that include manual, automatic or a combination of manual and automatic experimental means, the scope of which encompasses the above

described definition of a high throughput instrument. See Agrafiotis et al. Column 9, lines 49-56.

Instant claim 6 requires the incorporation of a second data set, a second interaction partner and a second modular computational module for predicting therapeutic properties of a chemical compound. Instant claim 16 further requires the incorporation of a third data set, a third interaction partner and a third modular computational model for predicting therapeutic properties of a chemical compound.

Agrafiotis et al. teaches an iterative method that allows for the repetition of the above described method steps in order to perform a second round of computational modeling to arrive at a prediction of properties for a given chemical compounds. See Agrafiotis et al. Column 52, lines 8-15 and Column 52, lines 27-29. The second round of computational modeling specifically allows for the use of different chemical compounds, a different specie of data describing the compounds, and a separate iterative computational module with regard to what was used in the first round of computational modeling. This allows for an embodiment of the invention where two, three or more separate rounds of modeling are performed by two, three or more computational modules to arrive at a prediction of properties on a set of chemical compounds.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agrafiotis et al. taken in view of Harrous et al.

Agrafiotis et al. teaches the use of automatic experimental means to provide data describing interacting compounds, such as a ligand-receptor pair, but does not specify the use of multi-channel or multi-cell calorimeters or measurements of changes in

enthalpy or a combination of changes in enthalpy, entropy and free energy in order to describe the interaction between two molecules.

Harrous et al. emphasizes the importance of selecting appropriate calorimetry instrumentation for investigations of molecular interactions in order to conserve materials and time (see Harrous et al.; page 97, first column, lines 6-13). Harrous et al. further specifies that energetic and kinetic studies must be used in complement to structural approaches in the characterization of biological macromolecules interacting with molecules of low molecular weight (see Harrous et al.; first paragraph of the Introduction). As recited in the abstract, Harrous et al. discloses a study that evaluates the use of a Gill titration calorimeter and demonstrates its utility in determining changes in enthalpy, entropy and free energy and how combinations of these values are used in describing the interaction between with several inhibitors that bind to beta-trypsin, a well known protein enzyme. The Gill calorimeter is consistent with a reasonably broad interpretation of a multi-channel or multi-cell calorimeter as it provides an automated high-throughput experimental means of analyzing multiple samples and provides thermodynamic data on the interaction between molecules. See (Harrous et al.; page 96, column two, line 37 to page 97, column one, line 3),

Taken in view of Harrous et al., it would be obvious to one skilled in the art to employ the methods taught by Agrafiotis et al. and incorporate the use of a multi-cell or multi-channel calorimeter to measure changes in enthalpy or a combination of the changes in enthalpy, entropy, and free energy in order to describe the interaction between a training compound and a first interaction partner.

Claims 1, 2, 6, 7, 11, and 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agrafiotis et al. taken in view of Korzekwa et al.

Agrafiotis et al. teaches utilizing one or more iterative computational modules in order to predict potential property values related to interacting compounds, such as ligand-receptor pairs, but does not specify the prediction of therapeutic or ADMET property values nor suggest a preferred combination of properties predicted by a given set of modules.

Korzekwa et al. teaches that a bottleneck exists in the drug discovery process which begins with lead compound optimization and that a primary consideration for related investigations in the area of lead development is a compounds metabolic fate. On this point, Korzekwa et al. propose overcoming the bottleneck through the use of predictive models which focus on absorption, distribution, metabolism, excretion and other pharmacokinetic properties, the set of which encompass ADMET properties (absorption, distribution, metabolism, excretion, and toxicological) as disclosed in the instant application. See Korzekwa et al.; column 1, lines 34-65. Further, it is explicitly asserted that "...it would generally be difficult to predict the effect of structural modification of a target compound upon its metabolism by enzymes, given that the molecular mechanisms of its metabolism involve an intimate combination of effects contributed by the metabolizing enzymes and the compounds themselves" (Korzekwa et al.; column 5, lines3-8).

In view of Korzekwa et al., it would be obvious for one skilled in the art to predict therapeutic and/or ADMET property values with the computational modules as taught by Agrafiotis et al. Further in view of Korzekwa, it would be obvious to one skilled in the art to predict therapeutic, ADMET and/or combinations of these properties with a combination of the computational modules taught by Agrafiotis et al. in order to address any intimate combination effects of the compounds under investigation.

Claims 1, 2, 6, 7, 8, 9, 11, and 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agrafiotis et al. taken in view of Korzekwa et al. and Ekins et al.

Agrafiotis et al. provides several embodiments of iterative computational modules that employ one of several varieties of QSAR model but does not specify the use of a 4D-QSAR model or that the model predict therapeutic property values. As discussed above, it would be obvious to one skilled in the art to predict therapeutic and/or ADMET property values using the iterative computational modules taught by Agrafiotis et al. taken in view of Korzekwa et al., but neither specify the use of a module that incorporates the use of a 4D-QSAR model.

Ekins et al., drawn to an investigation of the utility and quality of 3D- and 4D-QSAR models of Cytochrome P-450 3A4 inhibitors, suggests the importance of 4D-QSAR models for *in silico* prediction of properties describing interactions between molecules and asserts that in refining screening processes and accelerating drug

discovery applicable computational techniques, such as the 4D-QSAR model, are required. See Ekins et al.; page 429, Abstract and column 1, first full paragraph.

In view of Ekins et al. and Korzekwa at al., it would be obvious to one skilled in the art to incorporate a 4D-QSAR model into the computational module taught by Agrafiotis et al. for use in the prediction of therapeutic property values related to the interacting compounds under investigation.

Claims 1, 2, 6, 7, 9-11 and 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agrafiotis et al. taken in view of Korzekwa et al. and Khiat et al.

Agrafiotis et al. discloses a specific embodiment of the invention that involves the evaluation of inhibitors to the enzyme thrombin, a protein that serves as the interaction partner for a set of inhibitors, but does not disclose an embodiment of the invention where the interaction partner is a protein hormone or require that a module predict therapeutic property values. As discussed above, it would be obvious to one skilled in the art to predict therapeutic and/or ADMET property values using an iterative computational module taught by Agrafiotis et al. taken in view of Korzekwa et al., but neither specify the selection of an interaction partner which is a protein hormone.

Khiat et al. discloses that an initial structural analysis based on NMR constraints was insufficient in defining the interactions between a critical region of motilin, a protein hormone, with erythromycin A derivatives. Instead, an alternative structure-activity study was performed and relied upon to establish the structure and properties of key functional groups within motilin that interact with inhibitor molecules. Further, no studies

had been performed prior to Khiat et al. that relied on structure-activity comparisons with these specific compounds and protein hormone, suggesting that other investigations into protein hormone systems would benefit from similar structure-activity studies.

In view of Khiat et al. and Korzekwa at al, it would be obvious to one skilled in the art to employ the methods disclose in Agrafiotis et al. and predict therapeutic property values for systems where a protein hormone serves as the interaction partner.

Claims 1, 2, 6, 7, 11-13, and 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agrafiotis et al. taken in view of Korzekwa et al. and Klein et al.

Agrafiotis et al. provides several embodiments of iterative computational modules that employ one of several varieties of QSAR model but does not specify the use of an MI-QSAR model or that a module predict therapeutic property values. As discussed above, it would be obvious to one skilled in the art to predict therapeutic and/or ADMET property values using the iterative computational modules taught by Agrafiotis et al. taken in view of Korzekwa et al., but neither specify the use of a module that incorporates the use of an MI-QSAR model.

Klein et al. discloses how intermolecular membrane-interaction descriptors were derived from molecular dynamics simulations of the compounds in a model phospholipid monolayer and analyzed with an MI-QSAR model. See Klein et al., abstract. Further, Klein et al. asserts that very few structure-activity stidues for explicit membrane-interactions are available to date and despite the many efforts that have been made to

understand the molecular principles behind drug-phospholipid interaction. See Klein et al., Introduction, second full paragraph. This suggests that the MI-QSAR model is one of a very few structure–activity models capable of handling the demands of the many studies involving explicit membrane-interactions.

In view of Kleins et al. and Korzekwa at al., it would be obvious to one skilled in the art to incorporate an MI-QSAR model into the computational module taught by Agrafiotis et al. for use in the prediction of therapeutic and/or ADMET property values related to interacting compounds which involve explicit membrane-interactions.

Claims 1, 2, 6, 7, 11, and 13-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agrafiotis et al. taken in view of Korzekwa et al. and Oprea et al.

Agrafiotis et al. discloses a specific embodiment of the invention that involves the evaluation of inhibitors to the enzyme thrombin, a protein that serves as the interaction partner for a set of inhibitors, but does not disclose an embodiment of the invention where the interaction partner is a membrane, membrane-like compound or a membrane that is part of a Caco-2 cell nor suggest predicting therapeutic and/or ADMET property values. As discussed above, it would be obvious to one skilled in the art to predict therapeutic and/or ADMET property values using the iterative computational modules taught by Agrafiotis et al. taken in view of Korzekwa et al., but neither specify the selection of an interaction partner which is a membrane, membrane-like compound or a membrane that is part of a Caco-2 cell.

Oprea et al. sites that "Poor intestinal permeability of drugs constitutes a major bottleneck in the successful development of candidate drugs" and that the pressure felt by current medicinal and combinatorial chemists drives researchers to incorporate a QSAR paradigm for drug absorption properties, as exemplified in their disclosure drawn to a structure-activity study that specifically involved a Caco-2 cell membrane. See Oprea et al.; Abstract.

In view of Korzekwa et al. and Oprea et al. it would be obvious to one skilled in the art that membrane and membrane-like compounds, as exemplified in the specific use of Caco-2 cell membrane from Oprea et al., are sufficient for use in construction of a computational module as disclosed in Agrafiotis et al. for use in predicting therapeutic property values relevant to one or more ADMET property values

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Patents US-6,691,045 and US-6,587,845 both disclose methods for computational approaches to *in silico* drug discovery which employ similar computational means that use QSAR models.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. DeJong whose telephone number is (571) 272-6099. The examiner can normally be reached on Monday-Friday between the hours of 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

EDJ

ARDIN H. MARSCHEL
PRIMARY EXAMINER

11/26/04